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BIOENGINEERING

Kidney glomerulus-on-a-chip

In vitro models that mimic the glomerulus could aid understanding of glomerular disease processes and potentially guide therapeutic discovery. Researchers now report a method for directing the efficient differentiation of human induced pluripotent stem cells (iPSCs) into podocytes that can be co-cultured with human glomerular endothelial cells in an organ-on-a-chip microfluidic device. "Our functional *in vitro* model of the human glomerular capillary wall replicates the selective molecular filtration and glomerular filtration rate of the kidney, in addition to modelling drug-induced podocyte injury and proteinuria," explains Donald Ingber.

"We have previously published a model of the human kidney proximal tubule and showed that it can model cisplatin toxicity, but were unable to establish a model of the human kidney glomerulus," says Ingber. To address this issue, the researchers assessed the ability of environmental cues to induce the differentiation of iPSCs into podocytes, and found that in the presence of laminin and specific soluble factors, iPSCs differentiated into cells with the morphological and molecular characteristics of podocytes. To mimic the urinary and capillary compartments of the glomerulus, they cultured iPSC-derived podocytes and primary kidney endothelial cells in a microfluidic device on opposite sides of a porous laminin-coated membrane. The device was designed with parallel hollow channels to enable application of mechanical strain, mimicking blood pulsations in the living glomerulus. In the presence of fluid flow and mechanical strain, the podocytes extended their processes through the membrane pores towards the endothelium. The co-cultures demonstrated selective filtration by permitting the excretion of inulin into the urinary compartment while retaining albumin in the capillary compartment. Treatment of the chips with adriamycin, however, led to podocyte detachment and loss of albumin into the urinary compartment, highlighting the potential of this approach to study kidney disease mechanisms and nephrotoxicity *in vitro*.

Susan J. Allison

> "Our functional *in vitro* model of the human glomerular capillary wall replicates the selective molecular filtration and glomerular filtration rate of the kidney"

ORIGINAL ARTICLE Musah, S. *et al.* Mature induced-pluripotent-stem-cell-derived human podocytes reconstitute kidney glomerular-capillary-wall function on a chip. *Nat. Biomed. Eng.* **1**, 0069 (2017)